



Patent Application
Serial No. 08/519,293

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Group Art Unit 1808 :
In re Application of :
HITOSHI NAGAOKA : INHIBITOR OF HEPATITIS B
Serial No. 08/519,293 : AND HIV ACTIVITY
Filed August 25, 1995 :
Examiner - I. Marx :

DECLARATION-3

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

I, Hideo Sawadaishi, declare as follows:

1. I am a citizen of Japan, and residing at Sunny Homes Negishi B 101, Tsutsumidai 83, Noda-shi, Chiba-ken, Japan. I graduated from prefectural Shimizu Senior High School, Department of Industrial Chemistry in March 1975. From April 1975 through 1991, I was an employee of Noda Shokkin Kogyo K.K. where I engaged in various research and development projects concerning Lentinus edodes mycelium. Since 1991, I have been an employee of Nagaoka L.E.M. Laboratory Co., Ltd., and during this time, I have been engaged in research and development projects concerning Lentinus edodes mycelium.

2. I am familiar with the contents of the present invention as well as of the prior art references cited in the application.

3. My prior Declaration dated October 4, 1995, presents data comparing compositions prepared according to the method disclosed in Japanese Patent Publication No.

1-312980 to Iizuka et al. ("Iizuka '980") and prepared according to the presently claimed invention. The data set forth in Table C of the October 4, 1995 Declaration shows that the culture mixture produced according to Iizuka '980 (Experiment III) contained a low relative amount of protein (5.4%) and a high relative amount of fiber (25.1%). In contrast, the extract produced according to the claimed invention (Experiment IV) contained a high relative amount of protein (27.0%) and a low relative amount of fiber (0.07%). The dramatic differences between the culture mixture of Iizuka '980 and the extract of the present invention are due to the addition of water and enzymes and the filtering step performed in the practice of the claimed invention.

4. Iizuka '980 teaches use of a culture mixture containing fungus and bagasse as a healthy food. The purpose of the process disclosed in Iizuka '980 is to obtain a fibrous dietary product, hence the culture mixture has a high fiber content and low protein content.

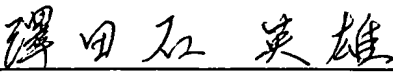
5. The present invention relates to a filtrate of a fungal culture to which extraneous enzymes and water were added. The final step in the claimed method removes the fungus and solid culture medium leaving an extract which the applicant discovered possesses anti-HIV activity. These key process steps of (1) adding enzymes and (2) filtering the medium to obtain an extract are responsible for the high protein content and anti-HIV activity of the extract.

6. A composition produced according to Iizuka '980 would not be expected to have efficacy against HIV because it is produced by a significantly different type of process from the claimed invention. If the Iizuka '980 composition were added to a culture of HIV-infected cells in an amount comparable to the efficacious amount of the extract produced according to the claimed invention is added to cultures of HIV infected

cells, the viability of such cells treated with the Iizuka '980 composition would not be expected to improve. This is because the culture mixture of Iizuka '980 is not produced by adding extraneous enzymes or separation of the fluid portion thereof. The extraneous enzymes are believed to release components essential to anti-HIV activity from the fungus into the culture medium. Upon filtration, the resulting filtrate contains the anti-HIV components in an efficacious concentration. Without the addition of enzymes or separation to obtain a filtrate, the surprising anti-HIV activity disclosed in the present application would not have occurred.

7. Any strain of the fungus Lentinus edodes is suitable for use in practicing the claimed invention. My prior Declaration reported results achieved using one strain of Lentinus edodes, and that strain was exemplary of all strains of Lentinus edodes. The anti-HIV efficacy of an extract produced according to the present invention is essentially unaffected by the strain of Lentinus edodes.

8. I declare further that all statements made herein of my own knowledge are true and that statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application and any patent issuing thereon.



Hideo Sawadaishi

Date May 11, 1998